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DOCKET NO.: CHEM0021US/ISIS-5799

Application No.: 10/561,324

Office Action Dated: August 5, 2008

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (currently amended) A composition comprising a first oligomeric compound and a second oligomeric compound, wherein:

the first oligomeric compound is complementary to and capable of hybridizing to the second oligomeric compound,

the first oligomeric compound is complementary to and capable of hybridizing and to a selected target nucleic acid,

one of the first and second oligomeric compounds comprises a plurality of linked nucleosides linked by internucleoside linking groups, and

the other at least one of the first and second oligomeric compounds comprises a plurality of linked nucleosides linked by internucleoside linking groups wherein essentially each of the nucleosides is has a 2'group that is other than 2'-OH and have has 3'-endo conformational geometry, and wherein at least one of the nucleosides having 3'-endo conformational geometry is a 2'-fluoro modified nucleoside comprising a purine heterocyclic base;

each of the first and second oligomeric compounds independently comprises from about 12 to about 30 nucleosides; and

wherein the composition optionally further comprises one or more phosphate groups, overhangs, stabilizing groups or conjugate groups.

- 2. (currently amended) The composition of claim 1 wherein the first oligomeric compound comprises the plurality of linked nucleosides linked by internucleoside linking groups wherein essentially each of the nucleosides is has a 2'group that is other than 2'-OH and have has 3'-endo conformational geometry.
- 3. (currently amended) The composition of claim 1 wherein the second oligomeric compound comprises the plurality of linked nucleosides linked by internucleoside linking groups wherein

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essentially each of the nucleosides is has a 2'group that is other than 2'-OH and have has 3'-endo

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conformational geometry.

4. (canceled)

5. (previously presented) The composition of claim 1 wherein each of the nucleosides of the

second oligomeric compound comprise a β -D-ribofuranose sugar group.

6. (previously presented) The composition of claim 1 wherein the 3'-terminus of the first

oligomeric compound comprises a stabilizing group.

7. (previously presented) The composition of claim 6 wherein the stabilizing group is a capping

group or a dTdT dimer.

8. (canceled)

9. (previously presented) The composition of claim 1 wherein the first oligomeric compound

comprises a 5'-phosphate group.

10-13. (canceled)

14. (previously presented) The composition of claim 1 wherein each of the internucleoside

linking groups of the first and second oligomeric compounds is, independently, a phosphodiester

or a phosphorothioate.

15-19. (canceled).

20. (previously presented) The composition of claim 1 wherein the 3'-terminus of the second

oligomeric compound comprises a stabilizing or conjugate group.

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21. (previously presented) The composition of claim 20 wherein the stabilizing group is a

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capping group or a dTdT dimer.

22. (previously presented) The composition of claim 20 wherein the 3'-terminus of the second

oligomeric compound comprises a conjugate group.

23-25. (canceled)

26. (currently amended) The composition of claim 1 wherein each of the nucleosides of the

first and second oligomeric compounds have has 3'-endo conformational geometry.

27-29. (canceled)

30. (currently amended) The composition of claim 1 wherein each of the nucleosides that are is

other than 2'-OH and have has 3'-endo conformational geometry comprises a 2'-substituent group

independently, selected from -F, -O-CH₂CH₂-O-CH₃, -O-CH₃, -O-(CH₂)₂-O-N(Rj)(Rj), -O-

 $(CH_2)_2$ -O- $(CH_2)_2$ -N(Rj)(Rj), -O- CH_2 -C(=O)-N(Rj)(Rj), -O- CH_2 -CH= CH_2 or and -O- $(CH_2)_3$ -

 $NH(R_i)$ where each R_i is, independently, H or C_1 - C_{10} alkyl.

31-38. (canceled)

39. (previously presented) The composition of claim 1 wherein the first and the second

oligomeric compounds are a complementary pair of siRNA oligonucleotides.

40. (previously presented) The composition of claim 39 wherein the first and the second

oligomeric compounds have 3'-dTdT overhangs.

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41. (previously presented) The composition of claim 39 wherein the first and the second

oligomeric compounds have blunt ends.

42. (previously presented) The composition of claim 1 further comprising at least one terminal

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cap moiety.

43. (previously presented) The composition of claim 42 wherein the terminal cap moiety is

attached to one or both of the 3'-terminal and 5'-terminal ends of the second oligomeric

compound.

44. (previously presented) The composition of claim 43 wherein the terminal cap moiety is an

inverted deoxy abasic moiety.

45-48. (canceled).

49. (previously presented) The composition of claim 1 wherein each of the first and second

oligomeric compounds has from about 12 to about 24 nucleosides.

50. (previously presented) The composition of claim 1 wherein each of the first and second

oligomeric compounds has from about 19 to about 23 nucleosides.

51-52. (canceled)

53. (withdrawn) A method of reducing target messenger RNA comprising contacting one or

more cells, a tissue or an animal with a composition of claim 1.

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54. (currently amended) The composition of claim 2 wherein each of the nucleoside <u>nucleosides</u> having 3'-endo conformational geometry comprises a <u>2'-F or 2'-O-CH₃</u> substitutuent group <u>2'-substitutuent group independently selected from F and O-CH₃</u>.

- 55. (currently amended) The composition of claim 54 wherein at least 7 of the <u>nucleosides</u> having 3'-endo conformational geometry comprises a 2'-O-CH₃ substitutent group 2'-substituent groups are -O-CH₃ and at least 12 of the <u>nucleosides having 3'-endo conformational</u> geometry comprises a 2'-F substitutent group 2'-substituent groups are -F.
- 56. (currently amended) The composition of claim 55 wherein the first oligomeric compound comprises is a compound of the formula:

$$5'-(N_f)_5(N_m)_2(N_f)_2(N_m)_2(N_f)_{5-6}(N_m)_3-3'$$

wherein:

each N_f is a 2'-F modified nucleoside; and each N_m is a 2'-OCH₃ modified nucleoside.